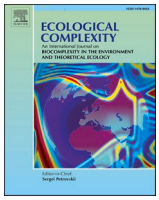
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Ecological Complexity 46 (2021) 100929

Contents lists available at ScienceDirect

Ecological Complexity

journal homepage: www.elsevier.com/locate/ecocom



A note on the impact of a behavioral side-effect of vaccine failure on the spread of a contagious disease

G.S. Harari [a], L.H.A. Monteiro [a,b,*]

[a] Universidade Presbiteriana Mackenzie,PPGEEC, São Paulo, SP, Brazil
[b] Universidade de São Paulo, Escola Politécnica, São Paulo, SP, Brazil

ARTICLE INFO

Keywords:
Basic reproduction number
Dynamical systems
Epidemic model
Vaccination failure
Vaccine efficacy

ABSTRACT

Vaccines do save lives; however, no vaccine provides complete immunity for all vaccinated individuals. Thus, some individuals remain susceptible to the contagious disease against which they were vaccinated. By relying on the supposed acquired immunity, these individuals can reduce the self-imposed prevention measures and, as a consequence, they can involuntarily promote the spread of the infection. Here, such individuals are taken into account in an epidemic model based on ordinary differential equations. Depending on the parameter values related to contagion and vaccine efficacy, a less responsible behavior post-vaccination can increase the basic reproduction number of the disease as compared to the case with no vaccine. This result is discussed by considering the current COVID-19 outbreak.

1. Introduction

Vaccines have increased our life expectancy throughout history (Domachowske and Suryadevara, 2021). Hence, in virtually all countries, immunization campaigns have been conducted by public health agencies (Domachowske and Suryadevara, 2021). Vaccines, however, are not perfect, in the sense of conferring a full long-term immunity for all vaccinated people (Heininger et al., 2012). Since the efficacy of any vaccine is below 100%, there always is a fraction of vaccinated people that remain unprotected. In addition, because they got the vaccine, these people think they are immunized. Thus, they can relax their preventive and protective measures and can be infected. Therefore, vaccinated-but-still-susceptible people, which are an outcome of vaccine failure, can increase the spread of a contagious disease. In this Short Communication, this issue is examined from a dynamical systems theory perspective. In Section 2, an epidemic model written in terms of ordinary differential equations (ODE) is proposed and analyzed. In Section 3, the relevance of this study is discussed by taking into consideration the ongoing COVID-19 pandemic.

2. The model and the analysis

Epidemic models based on ODE are suitable if the different groups of individuals composing the whole population are homogeneously distributed over the geographic region where they live (Anderson and May, 1992; Brauer et al., 2019; Keeling and Rohani, 2008). Assume that there is a contagious disease spreading in this region. In addition, assume that recovery confers a long-life immunity and vaccination against this disease confers a long-life immunity only for a fraction of this population (therefore, no immunity is elicited in the remaining fraction).

In epidemic models, vaccine failure usually corresponds to a non-null contagion rate for vaccinated individuals and/or no acquired immunity (Liu and Stechlinski, 2011; Wang et al. 2016). In this work, vaccine failure is taken into account on the vaccine efficacy and also as a behavioral side-effect. Hence, here, there are four distinct groups of individuals with different health statuses. The variables $S(t)$, $I(t)$, $R(t)$, and $S_v(t)$ respectively denote the numbers of susceptible individuals, infected individuals, immunized/recovered individuals, and individuals who were vaccinated but are still susceptible (that is, not immunized). Since the S_v-individuals have gotten the vaccine, they can suppose that they are immunized and, as a consequence, they can stop taking precautionary actions. Hence, the infection rate constant of the S_v-group is considered to be higher than the infection rate constant of the non-vaccinated S-group.

Assume that the numbers of individuals in these four groups vary with time t according to:

* Corresponding author.
E-mail addresses: gina.harari@mackenzista.com.br, szajnbokharari@hotmail.com (G.S. Harari), luizm@mackenzie.br, luizm@usp.br (L.H.A. Monteiro).

https://doi.org/10.1016/j.ecocom.2021.100929
Received 21 January 2021; Received in revised form 7 April 2021; Accepted 23 April 2021
Available online 15 May 2021

$$\frac{dS(t)}{dt} = -aS(t)I(t) - v_1S(t) - v_2S(t) + cI(t) + mR(t) + mS_v(t) \quad (1)$$

$$\frac{dI(t)}{dt} = aS(t)I(t) + \alpha S_v(t)I(t) - bI(t) - cI(t) \quad (2)$$

$$\frac{dR(t)}{dt} = bI(t) + v_1S(t) - mR(t) \quad (3)$$

$$\frac{dS_v(t)}{dt} = v_2S(t) - \alpha S_v(t)I(t) - mS_v(t) \quad (4)$$

In these equations, a and α are the infection rate constants of S and S_v-individuals, respectively, due to contact with I-individuals; b is the recovery rate constant of I-individuals; c is the death rate constant of I-individuals; m is the death rate constant of R and S_v-individuals; v_1 and v_2 are the rate constants related to successful and unsuccessful immunization of S-individuals due to vaccination, respectively. These seven parameters (a, α, b, c, m, v_1, and v_2) are positive constants. The differences in the behaviors and habits of S and S_v-individuals are taken into account by assuming that $\alpha > a$. The differences in the vaccination outcomes are expressed by the terms with v_1 and v_2: the term with v_1 excludes a vaccinated subpopulation from contagious events (that is, $S \rightarrow R$); the term with v_2 represents the kinetic jump to the vaccinated-but-still-susceptible group (that is, $S \rightarrow S_v$). Similar epidemic models based on ODE can be found in the literature (Anderson and May (1992); Brauer et al. (2019); Keeling and Rohani, 2008).

In the last years, the world population is growing at a rate of 1% per year (Worldometer, 2021). For simplicity, in this study, the total population size is supposed to remain unchanged; hence, the deaths of I, R, and S_v-individuals are balanced by the births of S-individuals (the deaths of S-individuals are also supposed to be balanced by the births of S-individuals; that is, these processes occur at equal rates. Therefore, because the corresponding terms cancel out, they do not appear in Eq. (1)). Note that the sum $dS(t)/dt + dI(t)/dt + dR(t)/dt + dS_v(t)/dt = 0$ implies $S(t) + I(t) + R(t) + S_v(t) = N$, in which N is the total number of individuals. Since $R(t) = N - S(t) - I(t) - S_v(t)$, then the original fourth-order system can be rewritten as the following third-order system of ODE:

$$\frac{dS}{dt} = -aSI - v_1S - v_2S + cI + m(N - S - I) = f_1(S, I, S_v) \quad (5)$$

$$\frac{dI}{dt} = aSI + \alpha S_vI - bI - cI = f_2(S, I, S_v) \quad (6)$$

$$\frac{dS_v}{dt} = v_2S - \alpha S_vI - mS_v = f_3(S, I, S_v) \quad (7)$$

The steady states (S^*, I^*, S_v^*) in the state space $S \times I \times S_v$, which correspond to time-independent solutions, are obtained from $dS/dt = 0$, $dI/dt = 0$, $dS_v/dt = 0$; that is, from $f_1(S^*, I^*, S_v^*) = 0$, $f_2(S^*, I^*, S_v^*) = 0$, $f_3(S^*, I^*, S_v^*) = 0$. This model has a disease-free steady-state (a stationary solution with $I^* = 0$) with coordinates:

$$(S^*, I^*, S_v^*) = \left(\frac{mN}{m + v_1 + v_2}, 0, \frac{v_2N}{m + v_1 + v_2}\right) \quad (8)$$

Its stability can be inferred from the eigenvalues λ of the Jacobian matrix $\mathbf{J}$, which is obtained by linearizing this system of ODE around this steady state. Such a state is locally asymptotically stable if the real part of all eigenvalues is negative (Guckenheimer and Holmes, 2002). In this case, $\mathbf{J}$ is given by:

$$\mathbf{J}(S^*, I^*, S_v^*) = \begin{bmatrix} -aI^* - v_1 - v_2 - m & -aS^* + c - m & 0 \\ aI^* & aS^* + \alpha S_v^* - b - c & \alpha I^* \\ v_2 & -\alpha S_v^* & -\alpha I^* - m \end{bmatrix} \quad (9)$$

For the disease-free solution, the eigenvalues (determined from $\det(\mathbf{J} - \lambda\mathbf{I}) = \mathbf{0}$, in which $\mathbf{I}$ is the identity matrix) are:

$$\lambda_1 = -v_1 - v_2 - m < 0 \quad (10)$$

$$\lambda_2 = aS^* + \alpha S_v^* - b - c \quad (11)$$

$$\lambda_3 = -m < 0 \quad (12)$$

Therefore, the disease-free solution is attracting; in other words, the infectious disease can be eradicated, only if $\lambda_2 < 0$.

The basic reproduction number (Anderson and May (1992); Brauer et al. (2019); Keeling and Rohani (2008); Schimit and Monteiro, 2012) of an epidemic model, denoted by R_0, can be viewed as a bifurcation parameter, because for $R_0 < 1$ the disease tends to naturally disappear and for $R_0 > 1$ the disease tends to endemically persist. Thus, the critical number $R_0 = 1$ is associated with a transcritical bifurcation. In this bifurcation, two steady states exchange their stabilities by varying a parameter value around a critical number (Guckenheimer and Holmes, 2002). Usually, the higher the value of R_0 (for $R_0 > 1$), the higher the amount of infected individuals in the endemic steady-state (a stationary solution with $I^* > 0$). The parameter R_0 is also interpreted as the average number of secondary infections caused by a single infected individual (Anderson and May (1992); Brauer et al. (2019); Keeling and Rohani (2008); Schimit and Monteiro, 2012). Its value depends on the infectious pathogen and on characteristics of the host population (such as density, lifestyle, mortality, natality, structure of health services, etc.).

The basic reproduction number of this model is defined as:

$$R_0 \equiv \frac{aS^*}{b + c} + \frac{\alpha S_v^*}{b + c} \quad (13)$$

because $R_0 < 1$ implies $\lambda_2 < 0$ (and, consequently, the disease is eradicated). This expression can be rewritten as:

$$R_0 = r_0\left(\frac{m}{m + v_1 + v_2}\right) + \frac{\alpha r_0}{a}\left(\frac{v_2}{m + v_1 + v_2}\right) \quad (14)$$

with:

$$r_0 \equiv \frac{aN}{b + c} \quad (15)$$

In the absence of vaccination, that is, for $v_1 = 0$ and $v_2 = 0$, r_0 is the basic reproduction number, as deduced in other works (Ferraz and Monteiro (2019); Schimit and Monteiro, 2009).

Eq. (14) reveals that if $v_1 > 0$ and $v_2 = 0$; that is, if the unimmunized group does not exist because the vaccine efficacy is 100%, then $R_0 = r_0[m/(m + v_1)] < r_0$. Therefore, for $v_2 = 0$, the vaccination is beneficial for any value of $v_1 > 0$, because it reduces the basic reproduction number. For instance, for measles, it is reasonable to consider $v_2 \approx 0$ (Holzmann et al., 2016). Suppose that the average life expectancy of the population is 80 years; thus, $m = 1/(80 \times 52)$, if the time t is measured in weeks. Eradication requires $R_0 = r_0m/(m + v_1) < 1$. By taking $r_0 = 18$ (Holzmann et al., 2016), then $v_1 > 0.004$; that is, at least 0.4% of the susceptible group must be vaccinated against measles per week in order to eliminate this disease.

If the vaccine efficacy is below 100%, then $v_2 > 0$, which can be associated with the emergence of a subpopulation having less responsible behavior. In this case, imperfect vaccine leads to $R_0 > r_0$ if:

$$\frac{m}{m + v_1 + v_2} + \frac{\alpha}{a}\left(\frac{v_2}{m + v_1 + v_2}\right) > 1 \quad (16)$$

Therefore, potentially dangerous behavior related to vaccine failure is harmful to the population if:

$$\alpha > \alpha_c \equiv \frac{a(v_1 + v_2)}{v_2} \quad (17)$$

This critical value of α, denoted by α_c, increases with the vaccine efficacy. For instance, for a vaccine with 50% efficacy, that is, $\nu_1 = \nu_2$, then $\alpha_c = 2a$; with 66.7% efficacy, that is, $\nu_1 = 2\nu_2$, then $\alpha_c = 3a$.

For $R_0 > 1$ and $\alpha > 0$, the system converges to the endemic steady-state given by:

$$\left(S^{'*}, I^{'*}, S_v^{'*}\right) = \left(\frac{N}{r_0} - \frac{\alpha S_v^{'*}}{a}, \frac{-y + \sqrt{y^2 - 4xz}}{2x}, \frac{\nu_2 N}{[(\nu_2\alpha/a) + m + \alpha I^{'*}]r_0}\right) \quad (18)$$

with $x = (b+m)\alpha$, $y = \alpha N(\nu_1 + \nu_2)/r_0 + mN(a+\alpha)/r_0 - (c-m)(m + \nu_2\alpha/a) - mN\alpha$, and $z = (\nu_1 + \nu_2)mN/r_0 - m^2N(r_0 - 1)/r_0 - mN\nu_2\alpha/a$. For $\alpha = 0$ and $\nu_2 = 0$, Ferraz and Monteiro (2019) had already shown that the endemic attractor is:

$$\left(S^{'*}, I^{'*}, S_v^{'*}\right) = \left(\frac{N}{r_0}, \frac{N(\nu_1 + m)}{(b+m)r_0}\left[\frac{mr_0}{\nu_1 + m} - 1\right], 0\right) \quad (19)$$

Fig. 1 illustrates these results. This figure was obtained by numerically solving Eqs. (1)-(4) with the 4th-order Runge-Kutta integration method with integration time step of 0.01. Take $N = 1$ (normalized population size), $a = 1$, $b = 1/2$, $c = 1/3$, and $m = 1/3$. These fictitious numbers were chosen to better visualize the impact of α, ν_1, and ν_2 on the epidemic course. Fig. 1 shows four plots of $I(t)/N$:

- black line: $\alpha = 0$, $\nu_1 = 0$, and $\nu_2 = 0$; in this case, $r_0 = 1.2$;
- green line: $\alpha = 3$, $\nu_1 = 1/10$, and $\nu_2 = 0$; in this case, $R_0 \simeq 0.92$;
- blue line: $\alpha = 1.5$, $\nu_1 = 1/10$, and $\nu_2 = 1/10$; in this case, $R_0 \simeq 1.09$;
- red line: $\alpha = 3$, $\nu_1 = 1/10$, and $\nu_2 = 1/10$; in this case, $R_0 \simeq 1.43$.

The black line corresponds to no vaccination. Since $r_0 = 1.2 > 1$, the disease becomes endemic. In this case, the simulation shows that $I(t)/N \to 0.067$ for $t \to \infty$, which is also the number found from Eq. (19).

The green line corresponds to vaccine efficacy of 100%. Since $R_0 \simeq 0.92 < 1$, the disease tends to disappear. In fact, in the simulation, $I(t)/N \to 0$ for $t \to \infty$, which is in accordance with Eq. (8).

The blue line corresponds to vaccine efficacy of 50% and $\alpha < \alpha_c = 2$. Note that the blue curve is below the black curve. In the simulation, $I(t)/N \to 0.027$ for $t \to \infty$, which is also the value determined from Eq. (18).

The red line corresponds to vaccine efficacy of 50% and $\alpha > \alpha_c = 2$. Note that the red curve is above the black curve. In this case, $I(t)/N \to 0.078$ for $t \to \infty$, which is also the number obtained from Eq. (18).

Therefore, depending on the values of α, ν_1, and ν_2, the risky behavior associated with imperfect vaccine can worsen the epidemic. Notice that, as expected, the endemic attractors obtained in the numerical simulations agree with those determined from the analytical expressions given by Eqs. (18) and (19).

A final remark: for COVID-19, plausible parameter values are $r_0 \simeq 3$, $b \simeq 1/3$, and $c \simeq 1/50$, if the time t is measured in weeks (Monteiro et al., 2020). For $N = 1$, then $a \simeq 1$ and $\alpha_c \simeq (\nu_1 + \nu_2)/\nu_2$.

3. Discussion and conclusion

The impact of vaccination has been theoretically studied since the seminal work by Daniel Bernoulli published in 1766 (Dietz and Heesterbeek, 2002). The key contribution of this Short Communication for this topic is Eq. (17). This expression was derived by considering that the homogenous mixing assumption holds, the population size does not vary, and that the rate constants related to contagion, death, recovery, and vaccination remain unaltered as the time progresses. Eq. (17) gives the critical contagion rate α_c of the S_v-group above which R_0 (the basic reproduction number with vaccination) is higher than r_0 (the basic reproduction number without vaccination). The beneficial effects of vaccination are undeniable; however, because no vaccine is perfect, everyone who got the vaccine should continue taking preventive measures (in order to keep $\alpha \leq \alpha_c$, and, consequently, $R_0 \leq r_0$).

Unfortunately, several epidemiological studies have conjectured

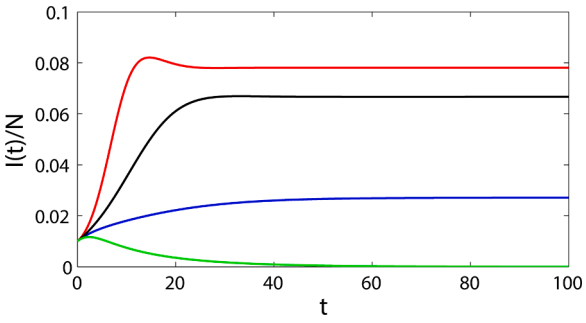


Fig. 1. Time evolutions of $I(t)/N$ for $N = 1$, $a = 1$, $b = 1/2$, $c = 1/3$, and $m = 1/3$ from the initial condition $S(0)/N = 0.99$, $I(0)/N = 0.01$, $R(0)/N = 0$, and $S_v(0)/N = 0$. Note that, for $N = 1$, $I(t)/N$ denotes the percentage of infected individuals at the instant t. For the black line, $\alpha = 0$, $\nu_1 = 0$, $\nu_2 = 0$, and $I(t)/N \to 0.067$; for the green line, $\alpha = 3$, $\nu_1 = 1/10$, $\nu_2 = 0$, and $I(t)/N \to 0$; for the blue line, $\alpha = 1.5$, $\nu_1 = 1/10$, $\nu_2 = 1/10$, and $I(t)/N \to 0.027$; for the red line, $\alpha = 3$, $\nu_1 = 1/10$, $\nu_2 = 1/10$, and $I(t)/N \to 0.078$.

that, after the pandemic phase, COVID-19 will endemically persist in our population as measles does (Fernandez and Zhu, 2021; John and Seshadri, 2021). These works advise that vaccinated individuals should not increase their mobility or stop wearing a face mask in public places. Thus, vaccine is only part of the solution. The other part is to act responsibly. Vaccination is a not a passport to selfish behaviors. Eq. (17) shows that the lower the vaccine efficacy, the lower the value of α_c. This study provides a mathematical basis for concerns about the possible negative aspects of low-efficacy vaccines on the global public health (Torreele, 2020; Vashishtha and Kumar, 2020).

CRediT authorship contribution statement

G.S. Harari: Software, Validation, Formal analysis, Investigation, Resources, Writing - original draft, Visualization, Funding acquisition, Data curation. **L.H.A. Monteiro:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing - original draft, Visualization, Funding acquisition, Writing - review & editing, Supervision, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

GSH thanks to Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for the scholarship. LHAM is partially supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) under the grant #304081/2018-3.

References

Anderson, R.M., May, R.M., 1992. Infectious Diseases of Humans: Dynamics and Control. Oxford University Press, Oxford.
Brauer, F., Castillo-Chavez, C., Feng, Z., 2019. Mathematical Models in Epidemiology. Springer, New York.
Dietz, K., Heesterbeek, J.A.P., 2002. Daniel Bernoulli's epidemiological model revisited. Math. Biosci. 180, 1–21.
Domachowske, J., Suryadevara, M., 2021. Vaccines: A Clinical Overview and Practical Guide. Springer, New York.
Fernandez, E.C., Zhu, L.Y., 2021. Racing to immunity: journey to a COVID-19 vaccine and lessons for the future. Br. J. Clin. Pharmacol. https://doi.org/10.1111/bcp.14686.
Ferraz, D.F., Monteiro, L.H.A., 2019. The impact of imported cases on the persistence of contagious diseases. Ecol. Complex. 40, 100788.
Guckenheimer, J., Holmes, P., 2002. Nonlinear oscillations. Dynamical systems, and bifurcations of vector fields. Springer, New York.

Heininger, U., Bachtiar, N.S., Bahri, P., Dana, A., Dodoo, A., Gidudu, J., dos Santos, E.M., 2012. The concept of vaccination failure. Vaccine 30, 1265–1268.
Holzmann, H., Hengel, H., Tenbusch, M., Doerr, H.W., 2016. Eradication of measles: remaining challenges. Med. Microbiol. Immunol. 205, 201–208.
John, T.J., Seshadri, M.S., 2021. COVID-19 endemicity: a taste of the future. Curr. Sci. 120, 266–267.
Keeling, M.J., Rohani, P., 2008. Modeling Infectious Diseases in Humans and Animals. Princeton University Press, Princeton.
Liu, X.Z., Stechlinski, P., 2011. Pulse and constant control schemes for epidemic models with seasonality. Nonlinear Anal. Real World Appl. 12, 931–946.
Monteiro, L.H.A., Fanti, V.C., Tessaro, A.S., 2020. On the spread of SARS-CoV-2 under quarantine: a study based on probabilistic cellular automaton. Ecol. Complex. 44, 100879.
Schimit, P.H.T., Monteiro, L.H.A., 2009. On the basic reproduction number and the topological properties of the contact network: an epidemiological study in mainly locally connected cellular automata. Ecol. Model. 220, 1034–1042.
Schimit, P.H.T., Monteiro, L.H.A., 2012. On estimating the basic reproduction number in distinct stages of a contagious disease spreading. Ecol. Model. 240, 156–160.
Torreele, E., 2020. The rush to create a COVID-19 vaccine may do more harm than good. BMJ-Brit. Med. J. 370, m3209.
Vashishtha, V.M., Kumar, P., 2020. Development of SARS-CoV-2 vaccines: challenges, risks, and the way forward. Hum. Vacc. Immunother. https://doi.org/10.1080/21645515.2020.1845524.
Wang, L.W., Liu, Z.J., Zhang, X.G., 2016. Global dynamics of an SVEIR epidemic model with distributed delay and nonlinear incidence. Appl. Math. Comput. 284, 47–65.
Worldometer (2021). Current world population. https://www.worldometers.info/world-population/(accessed 07 March 2021).